SOLUBILITY

Salt

Sugar

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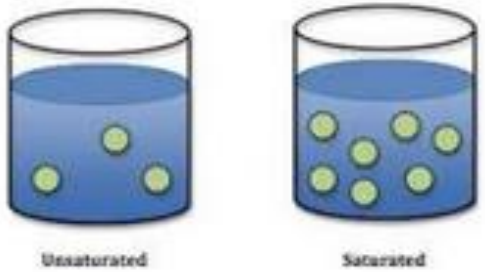
Definitions

- **Solution:** is a mixture of two or more components that form a homogenous mixture. The components are referred to the **solute and/or solutes** & the **solvent and/or solvents** .
- **Solute:** is the dissolved agent . (less abundant part of the solution)
- **Solvent** : is the component in which the solute is dissolved (more abundant part of the solution).
- **A saturated solution:** is one in which an equilibrium is established between dissolved and undissolved solute at a definite temperature. Or A solution that contains the maximum amount of solute at a definite temperature
- **An unsaturated solution:** or subsaturated solution is one containing the dissolved solute in a concentration below that necessary for complete saturation at a definite temperature.

Degree of saturation

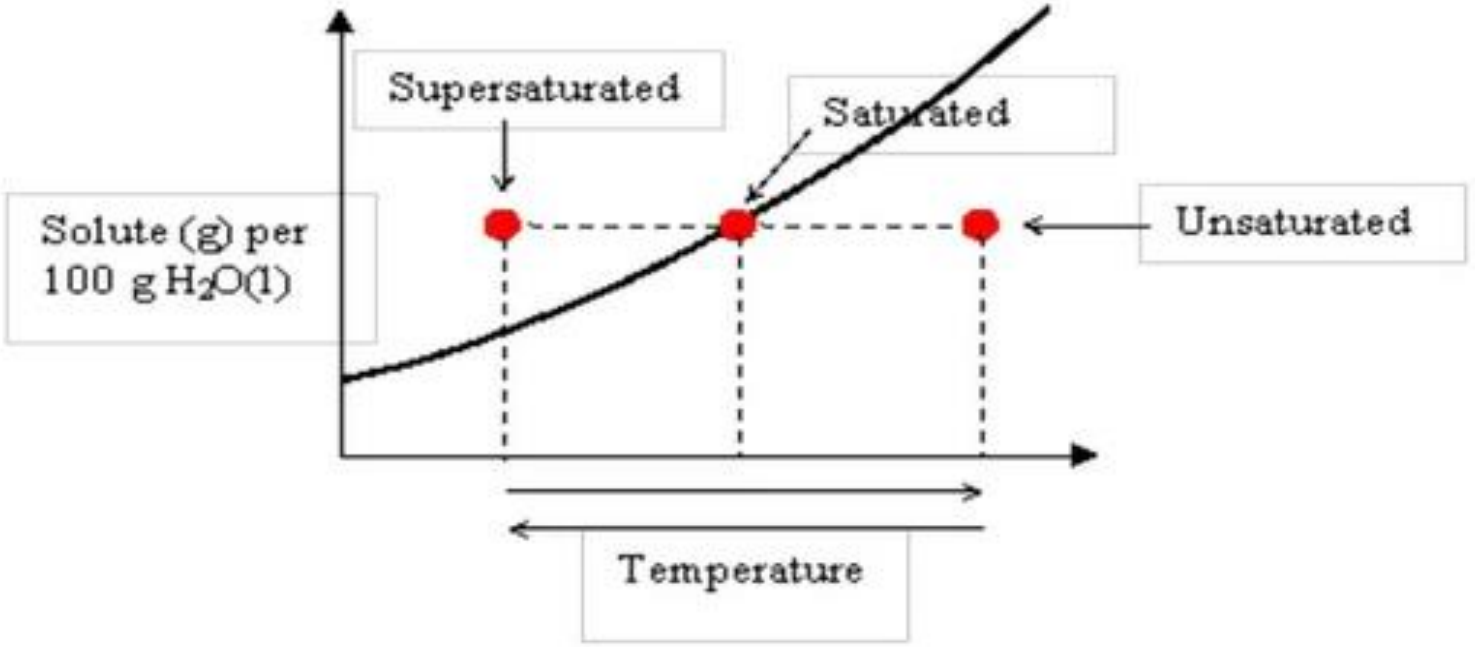


Unsaturated, Saturated or Supersaturated?

⇒ How much solute can be dissolved in a solution?

Solubility Curve

- Any solution can be made saturated, unsaturated, or supersaturated by changing the temperature.



Granulated sugar dissolves faster than sugar cubes, and both granulated sugar and sugar cubes dissolve faster in hot tea or when you stir the tea.

The compositions of the solvent and the solute determine whether or not a substance will dissolve.

Factors that affect how fast a substance dissolves include

- Agitation
- Temperature
- Particle size of the solute

Agitation

If the contents of the glass are stirred, the crystals dissolve more quickly. Agitation (stirring or shaking) affects only the rate at which a solid solute dissolves.

- The dissolving process occurs at the surface of the sugar crystals.
- Stirring speeds up the process because fresh solvent (the water) is continually brought in contact with the surface of the solute (sugar).

Temperature

Temperature also influences the rate at which a solute dissolves.

Sugar dissolves much more rapidly in hot tea than in iced tea.

At higher temperatures, the kinetic energy of water molecules is greater than at lower temperatures, so the molecules move faster

Particle Size of the Solute

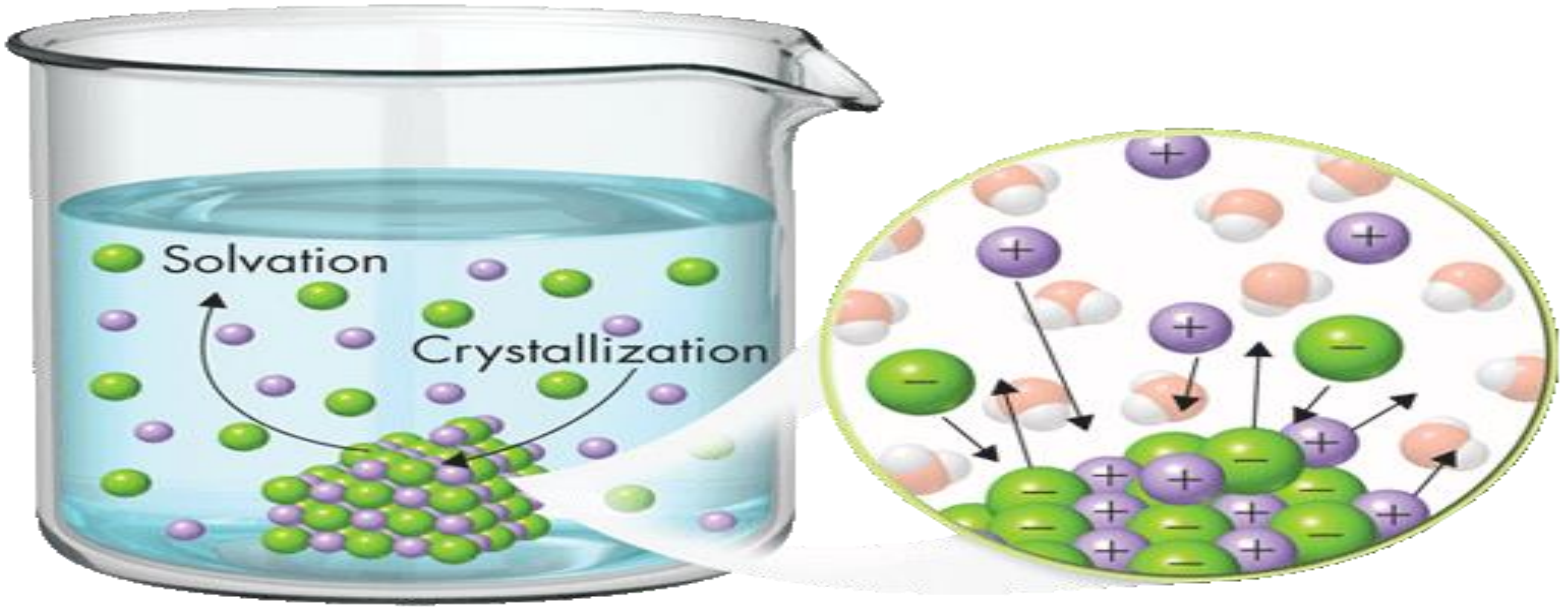
The rate at which a solute dissolves also depends upon the size of the solute particles.

- **The smaller particles in granulated sugar expose a much greater surface area to the colliding water molecules.**

- **The more surface area of the solute that is exposed, the faster the rate of dissolving.**

The dissolving process is a surface phenomenon

Saturated solution



A <u>saturated solution</u> contains the maximum amount of solute for a given quantity of solvent at a constant temperature and pressure.

In a saturated solution, a state of dynamic equilibrium exists between the solution and any undissolved solute, provided that the temperature remains constant.

Solubility expressions

The solubility of a substance is the amount of solute that dissolves in a given quantity of a solvent at a specified temperature and pressure to produce a saturated solution.

Descriptive terms	Relative amounts of solvents to dissolve 1 part of solute
Very soluble	Less than 1
Freely soluble	From 1-10
Soluble	From 10-30
Sparingly soluble	From 30-100
Slightly soluble	From 100-1000
Very slightly soluble	From 1000-10,000
Insoluble or practically insoluble	More than 10,000

Thermodynamic solubility of drugs

The thermodynamic solubility of a drug in a solvent is the maximum amount of the most stable crystalline form that remains in solution in a given volume of the solvent at a given temperature and pressure under equilibrium conditions.

The equilibrium involves a balance of the energy of three interactions against each other:

(1) solvent with solvent

(2) solute with solute

(3) solvent and solute

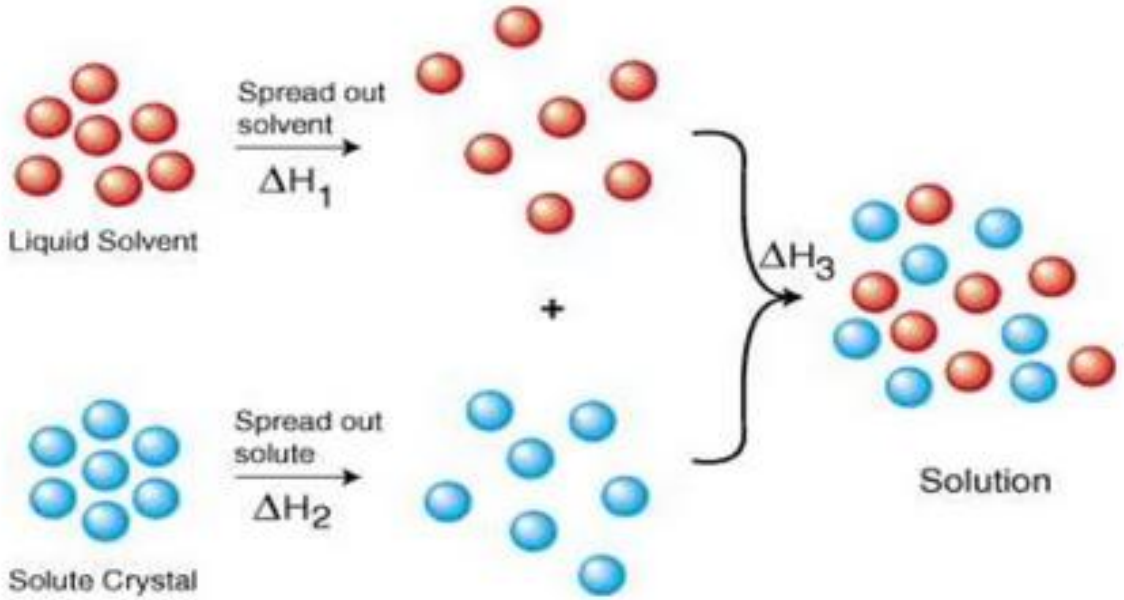
Solubility process

A mechanistic perspective of solubilization process for organic solute in water involves the following steps:

1. Break up of solute-solute intermolecular bonds
2. Break up of solvent-solvent intermolecular bonds
3. Formation of cavity in solvent phase large enough to accommodate solute molecule
4. Transfer of solute into the cavity of solvent phase
5. Formation of solute-solvent intermolecular bonds

types of interaction in the solution process

1. solvent – solvent interaction
2. solute – solute interaction
3. solvent solute interaction



$$\Delta H_{sol} = \Delta H_1 + \Delta H_2 + \Delta H_3$$

Enthalpy

- The enthalpy change of solution refers to the overall amount of heat which is released or absorbed during the dissolving process (at constant pressure).

- The enthalpy of solution can either be positive (endothermic reaction) or negative (exothermic reaction).

- The enthalpy of solution is commonly referred to as ΔH solution.

Solvent - Solute Interactions

- In pre - or early formulation, selection of the most suitable **solvent** is based on the principle of

"like dissolves like"

- That is, a solute dissolves best in a solvent with similar chemical properties. Or two substances with similar intermolecular forces are likely to be soluble in each others
- Polar solutes dissolve in polar solvents. E.g **salts & sugar dissolve in water .**
- Non polar solutes dissolve in non polar solvents. Eg**. naphtalene dissolves in benzene.**

Solute-Solvent interactions

- If the solvent is **A** & the solute is **B**, and the forces of attraction are represented by **A-A**, **B-B** and **A-B**,

One of the following conditions will occur:

1. If **A-A >> A-B** ⇨ The solvent molecules will be attracted to each other & the solute will be excluded. Example: Benzene & water, where benzene molecules are unable to penetrate the closely bound water aggregates.

2. If **B-B >> A-A** ⇨ The solvent will not be able to break the binding forces between solute molecules. Example NaCl in benzene, where the NaCl crystal is held by strong electrovalent forces which cannot be broken by benzene.

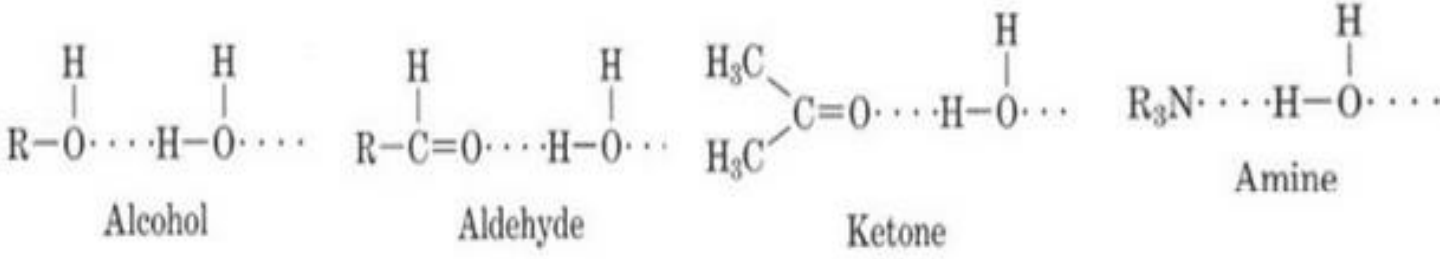
3. If **A-B >> A-A** or **B-B**, or the three forces are equal ⇨ the solute will . form a solution. Example: NaCl in water.

Polar solvents

- The solubility of a drug is due in large measure to the polarity of the solvent, that is, to its dipole moment. Polar solvents dissolve ionic solutes and other polar substances.

- The ability of the solute to form hydrogen bonds is a far more significant factor than is the polarity as reflected in a high dipole moment

Water dissolves phenols, alcohols and other oxygen & nitrogen containing compounds that can form hydrogen bonds with water.



Non polar solvents

- Non-polar solvents are unable to reduce the attraction between the ions of strong and weak electrolytes because of the solvents' low dielectric constants.
- They are **unable to form hydrogen bonds** with non electrolytes.
- Non polar solvents can dissolve non polar solutes through **weak van der Waals forces**
- **Example:** solutions of oils & fats in carbon tetrachloride or benzene.

Polyethylene glycol 400

Castor oil

Semi polar solvents

- Semi polar solvents, such as ketones can induce a certain degree of polarity in non polar solvent molecules. For example, benzene, which is readily polarizable, becomes soluble in alcohol
- They can act as **intermediate solvents** to bring about miscibility of polar & non polar liquids.

Example: **acetone increases solubility of ether in water.**

Propylene glycol has been shown to increase the mutual solubility of water and peppermint oil and of water and benzyl benzoate

Polarity as Dielectric Constant of Solvent, ε decrease , the solubility also decrease

Dielectric Constant of Solvent, ε (approx.)	Solvent	Solute
80	Water	Inorganic salts, organic salts
50	Glycols	Sugars, tannins
30	Methyl and ethyl alcohols	Caster oil, waxes
20	Aldehydes, ketones and higher alcohols, ethers, esters, and oxides	Resins, volatile oils, weak electrolytes including barbiturates, alkaloids, and phenols
5	Hexane, benzene, carbon tetrachloride, ethyl ether, petroleum ether	Fixed oils, fats, petrolatum, paraffin, other hydrocarbons
0	Mineral oil and fixed vegetable oils	

← Decreasing Polarity

← Decreasing Water Solubility